REMARKS

Claims 1-4, 8-9, 16, 19, 22, and 30-49 are pending. Claims 16, 19, 22, and 30-49 are allowed. Claims 1, 16, 19, 22, 30, 34, and 35 have been amended. The claims have been amended to more particularly and distinctly claim that which the Applicant regards as the invention.

In particular, Claim 1 and Claim 30 are amended to add the word "consisting" before the formula of the peptide and to correct an antecedent basis herein.

Claims 34 and 35 have been amended to replace the term "consisting essentially" with "consisting".

Claims 16, 19 and 22 have been amended to add the word "pharmaceutically" before the effective amount in these claims. Support for the pharmaceutically effective amount can be found in the specification, *inter alia*, at Page 17, last paragraph, where a typical dosage and regimen for the active agent of the pharmaceutical composition of the invention is disclosed.

The specification has been amended to insert the trademark registration symbol "®" at each occurrence of "Matrigel". Each occurrence of the mark has been capitalized.

The amendments to the claims do not constitute new matter as defined in 35 U. S. C. § 132. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application.

I. INTERVIEW WITH THE EXAMINER

The Applicant would like to extend their gratitude to the interview graciously granted by Examiner Low and Examiner Robinson to Applicant's attorney. In the interview, the Examiners suggested specific amendments to the claims to place the claims in better condition for allowance. These amendments include, addition of the word "consisting" before the formula of the peptide in Claim 1, replacement of the phrase "consisting essentially" with "consisting" in

Claims 34 and 35, and addition of the word "pharmaceutically" before the effective amount in Claims 15, 16, and 19.

In order to overcome the anticipation rejection of claims over Ferreira *et al.*, the Examiners requested a declaration by the inventor to provide evidence that the meaning of "N-terminal truncation fragment" of SEQ ID NO:1 and "C-terminal truncation fragment of SEQ ID NO:2" does not encompass peptides segments having randomly removed internal amino acids from SEQ ID NO:1 and SEQ ID NO:2, respectively. Submitted herewith is the Declaration of Keith R. McCrae, M.D. Under 37 C.F.R. § 1.132 ("McCrae Declaration"), establishing that the art-recognized meaning "N-terminal truncation fragment" and "C-terminal truncation fragment" do not encompassing molecules generated by random removal of internal amino acids from a parent peptide.

II. OBJECTION TO SPECIFICATION

The usage of the trademark MATRIGEL® has been objected to. The specification has been reviewed. Every occurrence of this mark has been capitalized, and the registration symbol inserted. Applicant disagrees that the MATRIGEL® mark is not accompanied by the relevant generic terminology. The specification identifies the product as "reconstituted extracellular matrix" at page 11, line 30.

III. REJECTION OF CLAIMS UNDER 35 U. S. C. § 102

A. REJECTION OF CLAIMS OVER FERREIRA *ET AL.*

On page 2, Paper No. 24, the Examiner maintains the rejection of Claims 1-4, 8-9 and 30-32 under 35 U. S. C. § 102 (b) as allegedly being anticipated by Ferreira *et al.* (WO 97/052258, February 13, 1997) for the same reasons as stated in the Office Action dated August 9, 2002 (Paper No. 18) and the Office Action dated March 25, 2003 (Paper No. 21). Specifically, the Examiner contends that Ferreira *et al.*'s peptide, represented by SEQ ID NO:

113 "Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val", anticipates Claims 1 and 30, wherein X is any amino acid, X_1 is the segment His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly (SEQ ID NO:1), or an N-terminal truncation fragment thereof containing at least one amino acid, and X_2 is zero amino acids.

Additionally, the Examiner contends that Ferreira *et al.*'s SEQ ID NO: 113 meets the limitations of Claim 2, which requires X_1 and X_2 to be from zero to six amino acids, and limitations of Claims 3-4, which requires X to be Phe, X_1 to be a fragment and X_2 to be two amino acids. Applicant respectfully traverses the Examiner's rejections for the following reasons.

Applicant respectfully submits that the Examiner's anticipation rejection of claims over Ferreira *et al.* is based on an improper interpretation of the expression "N-terminal truncation fragment" of SEQ ID NO:1" as including molecules generated by removing internal amino acids from SEQ ID NO:1. Contrary to the Examiner's assertion, an "N-terminal truncation fragment" of SEQ ID NO:1 does not encompass such molecules.

As Dr. McCrae states in his Declaration, "N-terminal truncation fragment" of SEQ ID NO:1 refers to a fragment generated by removing one or more amino acids contiguously from the N-terminus of SEQ ID NO:1, not random removal of amino acids from locations other than the N-terminal end of SEQ ID NO:1. As also stated by Dr. McCrae, "C-terminal truncation fragment" of SEQ ID NO:2 refers to a fragment generated by removing one or more amino acids contiguously from the C-terminus of SEQ ID NO:2, not random removal of amino acids from locations other than the C-terminal end of SEQ ID NO:2.

Applicant's response to the Office Action dated August 9, 2002 (Paper No. 18) and the Office Action dated March 25, 2003 (Paper No. 21) provided two tables (Table 1 and 2) that listed the amino acid sequences of the possible N-terminal truncation fragments and C-terminal truncation fragments of SEQ ID NOS:1 and 2, respectively. For the ease of reference, Table 1 is reproduced below.

Table 1 – POSSIBLE N-TERMINAL TRUNCATION FRAGMENTS OF SEQ ID NO:1

SEQ ID NO:1→ His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly

Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly

His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly

Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly

Gln-Gln-His-Gly-Leu-Gly-His-Gly

Gln-His-Gly-Leu-Gly-His-Gly

His-Gly-Leu-Gly-His-Gly

Gly-Leu-Gly-His-Gly

Leu-Gly-His-Gly

Gly-His-Gly

Gly

Table 1 shows that smallest N-terminal truncation fragment of SEQ ID NO:1 is the amino acid Gly. It is respectfully submitted that truncating SEQ ID NO:1 from the N-terminal to the maximum extent possible, *i.e.*, leaving only one original amino acid of SEQ ID NO:1, results in the single amino acid Glycine (Gly) as X_1. Thus, the peptide claimed in Claims 1 and 30 characterized by the minimal N-terminal truncation fragment is Gly-His-Lys-X-Lys-X_2. Accordingly, Ferreira *et al*'s peptide Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val does not anticipate the peptide of claims 1 and 30.

Claims 1 and 30 are not anticipated by the Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val (as SEQ ID NO:113) peptide of Ferreira *et al.* for yet another reason. X_2 in Applicant's X_1-His-Lys-X-Lys-X_2 peptide is (i) zero amino acids, (ii) the specific 12-amino acid sequence Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val (SEQ ID NO:2), or (ii) a C-terminal truncation fragment of SEQ ID NO:2 containing at least one amino acid. The C-terminal truncation fragments of SEQ ID NO:2 are generated by a truncation operation which starts at the C-terminal end of SEQ ID NO:2 and proceeds contiguously in the N-terminal direction removing one, two, three, etc. amino acids until one amino acid remains. All truncation possibilities encompassed within the

scope of the C-truncated peptides of Claims 1 and 30 are thus represented by the set of sequences of Table 2

Table 2 – POSSIBLE C-TERMINAL TRUNCATION FRAGMENTS OF SEQ ID NO:2

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val←SEQ ID NO:2

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln

Leu-Asp-Asp-Asp-Leu-Glu-His

Leu-Asp-Asp-Asp-Leu-Glu

Leu-Asp-Asp-Asp-Leu

Leu-Asp-Asp-Asp

Leu-Asp-Asp

Leu-Asp

Leu

To correspond to Ferreira *et al.*'s nonapeptide, Applicant's X_2 must be two amino acids. But it is clear from Table 2 that when X_2 is two amino acids in the claimed peptides, that two-amino acid sequence must be **Leu-Asp**. The corresponding two-amino acid sequence in the Ferreira nonapeptide is ***Asn-Val***. Similarly, for Applicant's X_1 to correspond to Ferreira's nonapeptide, Applicant's X_1 must consist of three amino acids. From Table 1, the three-amino acid sequence in the claimed peptides must be ***Gly-His-Gly***. The corresponding three-amino acid sequence in the Ferreira nonapeptide is **Glu-Ala-Pro**. The resulting claimed and Ferreira peptides are thus compared as follows:

Claimed	Gly-His-Gly-His-Lys- X -Lys-Leu-Asp
Ferreira *et al.*	Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val

Thus, it should be abundantly clear from the foregoing that Ferreira does not anticipate Claims 1-4, 8-9 and 30-32.

In view of the foregoing remarks, and in view of the McCrae Declaration, reconsideration and withdrawal of this rejection is respectfully requested.

B. REJECTION OF CLAIMS OVER JP07092171

On page 3, Paper No. 24, the Examiner rejects Claims 1 and 35 under 35 U. S. C. § 102(b) as allegedly being anticipated by (FARH) HOECHST JAPAN, Accession Number AAR75186, JP07082172-A 1995, (hereinafter, "JP07082172"). Specifically, the Examiner contends that JP07092171 discloses a formula wherein X is any amino acid, X_1 is a fragment thereof containing at least one amino acid and X_2 is zero amino acids. The Examiner believes that the JP07082172 formula encompasses the basic sequence "Gly-His-Lys-X-Lys" of the claimed invention. Additionally, the Examiner contends that JP07092171 discloses a compound that is 100% identical to the compounds claimed, as set forth in SEQ ID NO: 9 of this application. The Examiner alleges that because the claims recite the open ended languages "having" and "comprising," the elements of the claims are met by the reference, even though the reference compound is longer than the claimed polypeptides. Applicant respectfully traverses the Examiner's rejection.

Applicant respectfully submits that, as it is evident from the language of Claim 1, the transitional word "comprising" links different components of the claimed composition and clearly defines the scope of the pharmaceutical composition with respect to the elements such as a pharmaceutically acceptable carrier, and other active or inactive ingredients that may be

included in the pharmaceutical composition.[1] The word "comprising" does not open the scope of the formula in Claim 1.

Without acquiescing in the propriety of the Examiner's rejection, and solely to advance prosecution of this case, Applicant has amended Claims 1, and 35 to add the word "consisting" before the formula of the peptide in these claims.

Applicant respectfully submits that the peptides contained in the composition of Claim 1, as discussed above, require the minimal sequence Gly-His-Lys-X-Lys. The general formula of JP07082172 disclosing a formula wherein X is any amino acid, X_1 is a fragment thereof containing at least one amino acid, and X_2 is zero does not teach or suggest the peptide of Claim 1.

Moreover, Applicant respectfully submits that JP07092171 does not teach or suggest the compound of Claim 35 (SEQ ID NO: 9). The Examiner contends that this reference discloses a compound that is 100% identical to the compound represented by SEQ ID NO: 9 of Claim 35. Applicant was unable to find such compound in the disclosure and sequence listing of JP07092171. Accordingly, JP07092171 is not an anticipatory reference against this claim

In view of the forgoing remarks and the amendment to Claims 1 and 35, reconsideration and withdrawal of this rejection is respectfully requested.

C. REJECTION OF CLAIMS OVER JP08208692

On page 3, Paper No. 24, the Examiner rejects Claim 34 under 35 U. S. C. § 102(b) as allegedly being anticipated by (SUMU) SUMITOMO SEIYAKU KK, Accession Number AAW07625, JP08208692-A, 1996 (hereinafter, "JP08208692). Specifically, the

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[1] Of course, the other active ingredient may be a kininogen peptide *outside* the scope of the formula of Claim 1, the novelty of the claim being satisfied by the requirement that the composition contains at least one peptide *within* the bounds of the formula.

Examiner contends that JP08208692 teaches a compound that is 100% identical to the compound claimed and set forth in SEQ ID NO: 8 of the instant specification. The Examiner believes that because the claim contains the transitional word "having", the limitation of this claim is met by the reference, even though the compound disclosed by the reference is longer than the claimed compound. Applicant respectfully traverses the Examiner's rejection.

Applicant respectfully submits that the rejected claim does not recite the open ended language "having". Without acquiescing in the propriety of the Examiner's rejection, and solely to advance prosecution of this case, Applicant has amended Claim 34 to replace the phrase "consisting essentially" with the word "consisting" before the formula of the peptide in these claims.

Additionally, Applicant respectfully submits that JP08208692 does not teach or suggest the compound of Claim 34 (SEQ ID NO: 8). Applicant was unable to find such compound in the disclosure and sequence listing of JP08208692. Accordingly, JP08208692 is not an anticipatory reference against this claim.

In view of the forgoing remarks and the amendment to Claim 34, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

In light of the above, Applicant respectfully submits that all pending claims are allowable over the art of record, and a Notice of Allowance is courteously solicited. The foregoing is submitted as a full and complete response to the Office Action September 4, 2003 (Paper No. 24). The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,

KEITH R. McCRAE

BY _____

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Application No.: 09/437,912 Group Art Unit: 1653

Filed: November 9, 1999

For: INHIBITION OF ANGIOGENESIS BY HIGH MOLECULAR WEIGHT KININOGEN PEPTIDE ANALOGS THEREOF Examiner: H. Robinson

CERTIFICATE OF MAILING
UNDER 37 C.F.R. 1.8(a)

I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date indicated below, with sufficient postage, as first class mail, in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

BY Mo. Denise M. Collins

DATE: 1/30/04